AMENDMENT

Amendments to the Specification:

Following the abstract, please insert the attached Sequence Listing with subsequent page numbering thereafter.

Please replace paragraph [00062] with the following amended paragraph:

[00062] Figure 9 shows a sequence comparison of TrpC1 with other Trps which illustrates the conservation of a putative Homer ligand in the C-terminus. Modified from (Wes, 1995) (SEQ ID NO'S:25 to 30). (This should be updated with the largest set of Trp/VR1 family proteins that retain the PXXF [SEQ ID NO:3] motif.)

Please replace paragraph [00011] with the following amended paragraph:

[00011] The co-crystal determined that the EVH1 fold is isomorphic to the plextrin homology (PH) domain (Figure 1). The co-crystal also identified surfaces of interaction with the Homer ligand and rationalized the consensus sequence of the Homer ligand. Critical sites of contact include an association between the second proline (TPPSPF, SEQ ID NO: 2) and tryptophan W24 in the Homer 1 EVH1, and between the phenylalanine and a pocket that extends to glycine 89 of the EVH1 domain (Beneken et al., 2000). The critical contribution of these sites of interaction to the overall energetics of binding was confirmed in assays of binding that used point mutants of the EVH1 domain. The crystal also indicated that the original consensus sequence PPXXFR (SEQ ID NO:21) should be modified to PXXF ~~(SEQ ID NO:4)~~ (SEQ ID NO:3) since the first proline is not essential for contact with the EVH1 domain. The first proline may contribute to the overall conformation of the local protein sequence. The contact at the second proline involves the amino acid backbone and not the proline side chain, so other amino acids could, in principle, substitute for proline. Additional prolines are common in natural Homer ligands and are rationalized to be important in defining the correct configuration of the ligand for binding, but not in direct contact with the EVH1 binding surface. Perhaps most importantly, the co-crystal demonstrated that the

binding surface of the proline is similar to that of related EVH1 domains of Ena, Mena and Vasp, but the surface for the phenylalanine is unique to the Homer subfamily. Thus, it has been concluded that the Homer genes are a subfamily of the EVH1 family which possess unique binding surfaces and ligand sequence recognition.

Please replace paragraph [00092] with the following amended paragraph:

[00092] The nucleotide coding sequence of the Homer protein isolated from rat brain is shown in FIG. 18 as SEQ ID NO:6. The coding sequence has an open reading frame (ORF) of 558 nucleotides (FIG. 18; SEQ ID NO: 6). A 6.5 kb mRNA derived from this DNA encodes a 186 amino acid protein (FIG. 19; SEQ ID NO: 7). A long 3' UTR (Acc. No. U92079) encodes multiple AUUUA (SEQ ID NO:8) repeats, such as have been implicated in mRNA destabilization of immediate early genes (IEG). The amino acid sequence predicts a soluble protein that contains a single GLGF (SEQ ID NO:22) sequence and a preceding arginine (FIG. 7), a so-called "PDZ-like domain" which is predicted to have certain binding properties, based on its characterization in different, unrelated proteins, such as PSD-95.

Please replace paragraph [000169] with the following amended paragraph:

[000169] The hypothesis that Homer binds a proline rich sequence in the C-terminus of a family of membrane ion channels termed the Trp channels (Montell et al., 2002; Montell et al., 2002) was examined next. Trp channels are named for the first described member that is the basis for transient receptor potential in Drosophila phototransduction (Montell, 2001) and are nonspecific cation channels. This family is now recognized to include Trp channels that mediate influx of extracellular calcium, and VR1 subfamily proteins that mediate pain and temperature sensation (Figure 8) (Clapham et al., 2001). The sequence LPXPF ~~(SEQ ID NO:12)~~ (SEQ ID NO:23) is conserved in many members of the Trp channel family (Figure 9) (Montell, 2001), and conforms with the Homer consensus sequence PXXF (SEQ ID NO:3).

Please replace paragraph [000173] with the following amended paragraph:

[000173] Further analysis of Homer binding to TrpC1 revealed a second binding site in the N-terminus. During analysis of Homer binding to TrpC1 it was discovered that an N-terminal

fragment of TrpC1 also binds Homer. By generating and testing a series of deletion mutants, a second site of interaction was mapped to a sequence present in the N-terminus of TrpC1; LPSSPSSSSP (SEQ ID NO:5). An absence of a phenylalanine in this region was observed, suggesting that the binding interaction may be different from previously described Homer interactions. Mutation of prolines from LPSSPSSSSP ~~(SEQ ID NO:5)~~ (SEQ ID NO:24) to LASSPSSSSP (SEQ ID NO:5) or LPSSASSSSP (SEQ ID NO:17) resulted in TrpC1 mutants that no longer interacted with GST-Homer 3 EVH1 (Figure 12, right). By contrast, mutation to APSSPSSSSP (SEQ ID NO:18) or LPSSPSSSSA (SEQ ID NO:19) did not reduce binding to Homer. Together, these observations suggest a consensus of PSSP (SEQ ID NO:4).